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(54) Abstract Title
Sealing multiple arrays of reaction vessels, each with rim flange and seal, generally simultaneously with a single closure member

(57) An apparatus, such as laboratory reaction apparatus, comprises a multiple array of reaction vessels 40 (indicates a single such vessel), each of which has a flange 42 at or adjacent, and seal 43 associated with, an opening or a rim defining an opening of each vessel. The multiple vessel array is supported by a support member 30, relative to which is moveable, a closure member 20, which can be urged towards the rim of each reaction vessel 40, generally simultaneously to effect a fluid tight union between the reaction vessels 40 and the closure member 20. The apparatus may feature a plurality of such arrays and supporting features, shown in their closed configurations 2,3,4. Additional supporting features may include a temperature control block 50 with a hole 51 for each reaction vessel 40 and a gas manifold 26 and actuator 28 associated with the closure member 20. Several variations in the configuration of the flange 42 and seal 43 are disclosed across figures 2b-2h, which may additionally include a septum (23, fig.2g) enabling sampling / dosing of a reaction, or a safety bursting disc (24, fig.2h) mounted in a recess (25, fig.2h) of the closure member 20. The invention extends to physical and chemical processes carried out using the aforementioned apparatus comprising such steps as orbital shaking, stirring with rods, use of ultrasound, and heating or cooling.

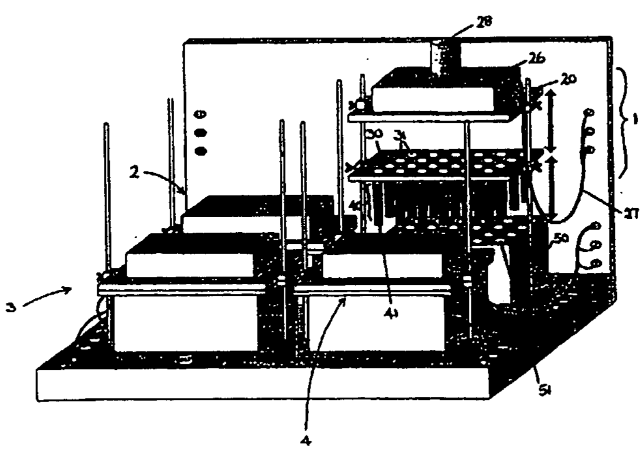
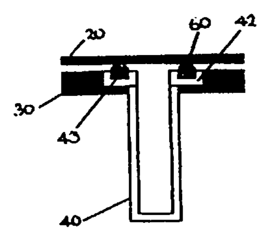


Figure 1



2a

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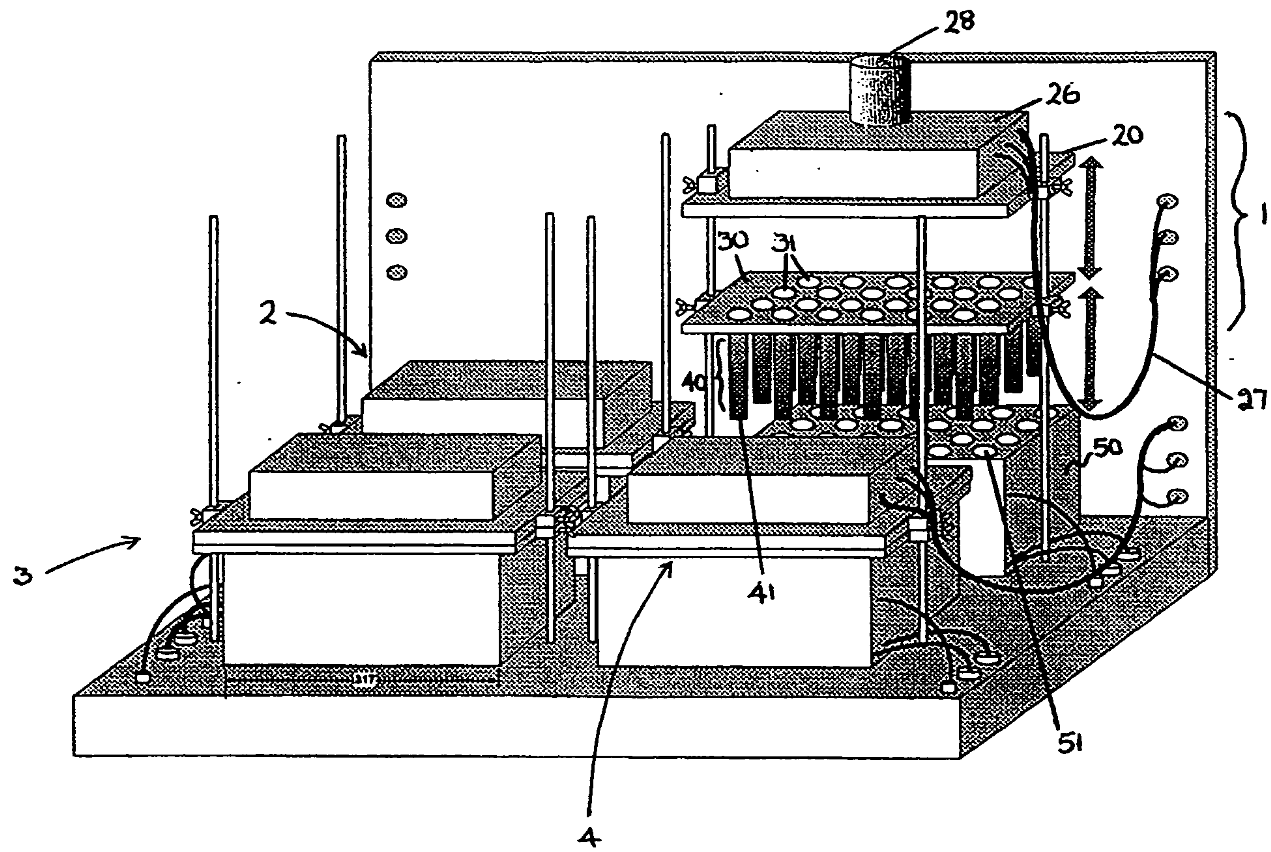
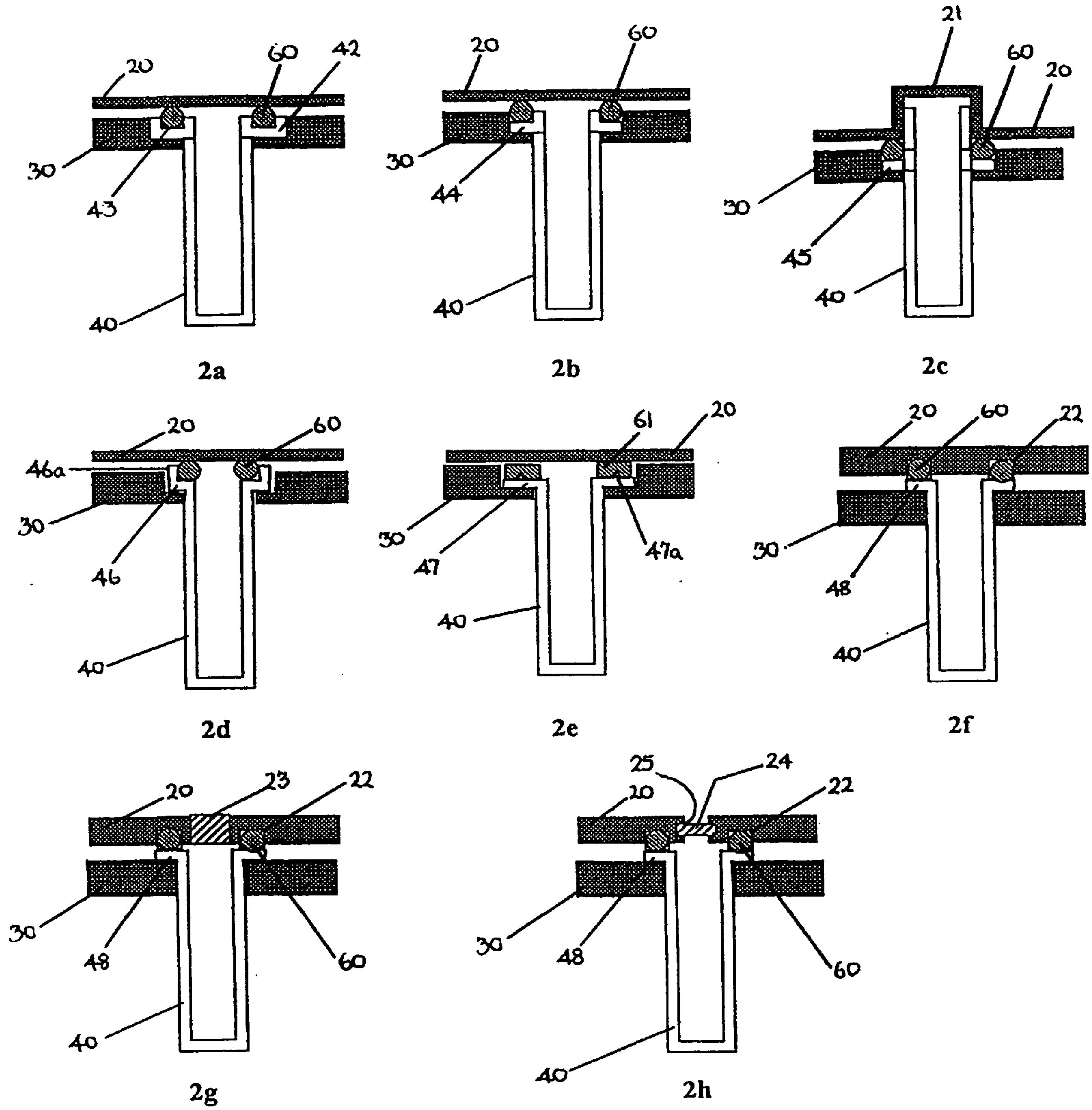


Figure 1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2b
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2c
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46a
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46
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2d
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47
47a
40
2e
20
60
22
30
48
40
2f
20
23
22
30
48
60
40
2g
25
24
20
22
30
48
60
40
2h

Figure 2

MULTIPLE VESSEL ARRAY

The present invention relates to a reactor vessel array in which a number of different physical and/or chemical operations can be performed, either simultaneously or sequentially. In particular, the present invention relates to an array of reactor vessels which are flanged and which have sealing means associated with the flange to facilitate sealing of all the vessels in the array in a single operation.

The desirability of performing a multiplicity of operations in a short time is well known to persons skilled in the art and a number of systems have been proposed with the aim of decreasing the time required for carrying out physical and/or chemical operations, including the time taken to deliver reaction products or effluent to an analyser. Some of the proposed systems also reduce the size or scale at which these operations are performed. Some such systems are commercially available and reference is made here to the CombiTec System introduced by Argonaut Technologies in which use is made of a so-called "Reactor Cassette".

One of the problems still remaining in this rapidly-

growing area of technology is how to carry out operations at elevated temperature and/or elevated pressure. Another problem that still has not been solved is how to deal satisfactorily with reactive components, possibly also at elevated temperature and/or elevated pressure.

It has already been proposed in International Patent Application No. WO98/36826 to use multi-autoclaves for the combinatorial synthesis of zeolites and other materials. The system disclosed in this document uses a central block containing a number of separated chambers provided with top and bottom plates and closing mechanisms which can be integrated with the central block. It is not possible to exchange the reactor vessels in the disclosed arrangement.

In International Patent Application No. WO98/56506, individual racks of reactor vessels are installed in a modular construction accommodating parallel racks in an array. A single lid, hinged on the reactor, is used to form a seal between a fluid manifold and all of the reactors at once. The integrity of the seal is ensured by using a spring or other biasing element to force the reactor onto the manifold. This acts as an intrinsically safe pressure regulator for operation upto 110-138 kPa

(16-20 psi), but the sealing mechanism cannot be used reliably at higher pressures.

International Patent Application No. WO99/24160 discloses an arrangement in which parallel racks of reactor vessels containing a reaction mixture, which can be dosed using a robot equipped with a syringe, are heated with a heated medium and simultaneously mixed in a shaker. The key to this concept is a novel flexible connection between the reactor tube and an overhead gas manifold through which a syringe can be deployed to add or remove fluids. Again, the sealing arrangement disclosed in this document does not lend itself to high-pressure applications.

In European Patent Application No. 0 916 397, an apparatus and method are disclosed for use in multiple simultaneous synthesis of general compounds. The system could, in principle, be used for high-pressure applications, but requires that each reactor vessel be opened and closed individually *via* a screw-cap fitting. Independent sealing of the reactor vessels in this way means that the system is not suitable for high throughput operations.

International Patent Application No. WO98/17391 describes

a system for the parallel handling of a plurality of vessels that are located on either side of a plate and are connected with each other *via* openings in the plate. The vessels are held in place with o-rings which are located in the plate openings and the vessels must be sealed individually. There is no common mechanism for sealing the vessels collectively. In addition, the seal design is not applicable to high-pressure operations.

From the foregoing, it can be seen that the main disadvantages of currently available systems are as follows:

- Limited flexibility - usually, the reaction vessels must be sealed individually. In addition, a number of the known systems only allow the use of specially designed components, which ties the user to a particular system manufacturer.

- The use of a screw-cap closure or of a spring/biasing component to achieve the necessary force for effective sealing. These mechanisms must be present for each individual reaction vessel.

- Suitability only for low-pressure applications.

- The use of cold reaction vessel lids may result in condensation of reagents during reaction. This is especially problematic for systems intended to work with only small volumes of fluid.

It is therefore an objection of the present invention to provide a reactor vessel array that has the capability for flexible exchange of reactor vessels, including different shapes or dimensions and possibly reaction vessels made of different materials. It is another object of the present invention to provide a reactor vessel array that allows easy exchange of reactor vessels in order that they may be used in another, consecutive, process or unit operation. It is yet another object of the present invention to provide a reactor vessel array which allows flexible exchange of inlet and outlet ports. It is still another object of the present invention to provide a reactor vessel array which has the capability to permit overhead stirring. It is a still further object of the present invention to provide a reactor vessel array which has separate inlets and outlets for gases, liquids and solids. Yet another object of the present invention is to provide a reactor vessel array which is adapted for high-pressure sealing. It is yet

another object of the present invention to provide a reactor vessel array which has the capability for sealing a plurality of reactor vessels in a single operation. A still further object of the present invention is to provide a reactor vessel array which is compatible with commercially available glassware, polymer containers, heaters and stirrers.

The invention is a multiple vessel array comprising a plurality of reaction vessels, a supporting plate having an array of reaction vessel holding formations, and a closure plate adapted for movement relative to said supporting plate such that it can be pressed against a rim of each of the reaction vessels to effect a fluid tight union between the reaction vessels and the closure plate, wherein said reaction vessels have a flange at or adjacent to the rim and a seal associated with the flange.

The advantage of this arrangement is that the reaction vessels are held by the supporting plate in such a way that they are prevented from falling through the supporting plate and therefore there is no need for an additional vessel holder underneath the supporting plate.

Preferably, the reaction vessels protrude through the supporting plate and are receivable in a temperature-controlled block which is moveable relative to the underside of the supporting plate to enable the reaction vessels to be placed within the environment of the block for uniform heating and/or cooling, as required.

Most conveniently, the reaction vessels are essentially tubular and have a transverse flange at or near the rim of the tube. However, it is also possible to use reaction vessels having shapes other than tubular. For example, the reaction vessels may be flasks of conical or spherical shape having their necks fitting the reaction vessel holding formations in the supporting plate. This increases the flexibility of the reaction vessel array according to the present invention. A flange-retaining collar may be required to assist in fastening non-tubular reaction vessels to the supporting plate.

If desired, the reaction vessels may be provided with inert linings which can either form an integral part of the insides of the reaction vessels or can be in the form of removable linings, for instance, linings made from chemically inert materials such as glass or plastics. If the reaction vessel wall is made of steel, for instance,

then an inert lining will be useful to prevent contact of the wall with aggressive reaction constituents. For example, when corrosive materials like hydrochloric acid have to be placed in steel vessels because of pressure requirements, an inert lining may be used to protect the reaction vessel walls.

Preferably, the seals associated with the reaction vessel flanges are O-ring seals. Alternatively, the seals may be formed of a material capable of forming a knife-edge which, when subjected to the closing force exerted by the closure plate, bites into the material of the flange, or of the closure plate, to establish an effective seal. In a variant of this arrangement, the flange could be formed with a knife edge which bites into the material of the seal, preferably a metal gasket formed of brass, gold, tantalum, iridium or the like, when subjected to the closing force exerted by the closure plate.

The supporting plate and the closure plate can be formed of any material compatible with the physical and/or chemical operations to be performed and may therefore comprise wood, glass, plastics, steel or the like. Preferably, the supporting plate and the closure plate are composed of steel. However, those skilled in the art

will be capable of choosing a suitable material depending on the nature of the operation(s) to be performed and it is not the purpose of this specification to teach the criteria used in such a selection process.

Because the supporting plate can be relatively short in comparison to the total length of the reaction vessels which it holds, the supporting plate is relatively light in weight compared to equivalent features in known apparatus.

Advantageously, the closure plate may incorporate septum means in alignment with each of the reaction vessel openings, to enable liquid sampling whilst maintaining seal integrity. Also, it is possible to incorporate a bursting disc in alignment with each of the vessel openings, for added safety.

The arrangement of the supporting plate and a closure plate enables good thermal contact between the temperature-controlled reaction block and the closure plate. This means that the closure plate, and hence the "lid" of each reaction vessel, may therefore be operated at approximately the same temperature as the temperature-controlled block. This reduces problems associated with

condensation of high-boiling components on the underside of the closure plate. The flange formations on the reaction vessels allow for flexible exchange of reaction vessels for others with different shapes or dimensions or that are composed from different materials. This flexible exchange capability also means that it is easy to exchange reaction vessels in order to use the same vessels in another, consecutive, process or unit operation. The capability also exists for flexible exchange of connections for inlet and outlet ports. The design of the closure plate may be such that there are separate inlets and outlets for gases, liquids and solids.

The simplicity of the design ensures that the components of the system are compatible with commercially-available glassware or reaction vessels of alternative materials such as plastics, and ensures compatibility with commercially available heaters and stirrers. Since the reaction vessels have a common closure plate rather than reactive lids which must be individually rotated or moved, the closure plate may have a variety of components mounted on it for monitoring or adjusting the progress of the reactions taking place in the reaction vessels. For example, these components could include temperature and

pressure sensors, pH electrodes and overhead stirrers.

The main advantage of the invention is that there is easy sealing of a multiplicity of reaction vessels by a single action. This single action sealing for all reaction vessels enables the use of convenient sealing mechanisms, which may be mechanically, electrically or pneumatically actuated. The robust nature of the construction means that reactions may be carried out at very high pressures. Operation is inherently safe due to the robust mounting of the flanged reaction vessels in the supporting plate.

The invention will now be particularly described by way of example only with reference to the drawings, in which:

Fig. 1 is a perspective view of (part of) a multiple vessel reaction apparatus; and

Fig. 2 is a series of cross-sectional views illustrating various sealing configurations for flanged reaction vessels.

In Fig. 1, a reactor vessel array 1 is shown in a partly exploded perspective view. Three other reactor vessel

beds 2, 3 and 4 are shown in the closed configuration. Multiple beds may be desirable, for example, where parallel reactions are being carried out under different conditions of temperature and/or pressure.

The reactor vessel array 1 comprises a closure plate 20 and a supporting plate 30 having a plurality of through-holes 31 each of which holds a reaction vessel 40. Each reaction vessel 40 has an elongate portion 41 depending from the underside of the supporting plate 30. The elongate portion 41 of each reaction vessel 40 is receivable in a hole 51 formed in a temperature-controlled block 50. In the example illustrated in Fig. 1, there are 24 reaction vessels arranged in a 6 x 4 array. The through-holes 31 in the supporting plate 30 are arranged to be in axial alignment with the holes 51 in the temperature-controlled block 50. It will be understood by a person skilled in the art that different sizes and dimensions of array could be used as an alternative without detriment to the performance of the invention.

The closure plate 20 has associated therewith a gas manifold 26 which is connected to a main fluid manifold (not shown) by connecting lines 27. The gas manifold 26

incorporates a number of pneumatically-actuated valves for controlling flow of gases to and from the reaction vessels 40. The actuator for the valves in the gas manifold 26 is denoted by reference numeral 28.

Turning now to Fig. 2, views 2a to 2h each show a cross-sectional view through a part of a reaction vessel array and depict different configurations of sealing between an individual reaction vessel 40 and the closure plate 20. For convenience, the reaction vessels 40 shown in these views are essentially tubular, although it will be understood by persons skilled in the art that other shapes of reaction vessel could be used provided that the neck formation in the region of the flange is compatible with the arrangements shown in these drawings.

Dealing firstly with view 2a, this represents one of the simplest arrangements for sealing the rim of a reaction vessel 40 to the underside of the closure plate 20. At the upper rim of the reaction vessel 40, there is a transverse flange 42 having a recess 43 described in its upper surface for receipt of an O-ring seal 60. When bedded into the recess 43, the O-ring seal 60 stands proud of the rim of the reaction vessel 40 so that, when the closure plate 20 is moved into sealing engagement

with the reaction vessel 40, fluid-tightness is effected by compression of the O-ring seal 60 between the underside of the closure plate 20 and the upper surface of the flange 42.

View 2b shows a variant that uses a reduced external flange 44. Rather than having a full transverse flange with a recess 43 like the variant depicted in view 2a, the reduced external flange 44 has no recess. Instead, the O-ring seal 60 is accommodated in the angle between the upstanding rim of the reaction vessel 40 and the transverse shelf formed by the flange 44. As previously, the O-ring seal 60 stands proud of the rim of the reaction vessel 40 so that, when the closure plate 20 is moved into sealing engagement with the reaction vessel 40, fluid-tightness is effected by compression of the O-ring seal 60 between the underside of the closure plate 20 and the upper surface of the flange 44.

View 2c shows another variant having an external flange 45. However, in this arrangement, the external flange 45 is positioned a short distance away from the rim of the reaction vessel 40 and the rim of the reaction vessel 40 protrudes into a blind hole 21 formed in the closure plate 20. In cross-section, one might say that the

closure plate 20 with its blind hole 21 forms a "top hat" section. The O-ring seal 60 no longer stands proud of the rim of the reaction vessel 40, but engages the underside of the closure plate 20 at the intersection of the rim and the base of the crown of the top hat section.

View 2d shows an arrangement having a reduced internal flange 46. Here, the rim of the reaction vessel 40 merges directly into the transverse flange 46 which has an upstanding lip 46a at its radially outermost periphery. The O-ring seal 60 is accommodated radially inwardly of the upstanding lip 46a and overlies the rim of the reaction vessel 40. The O-ring seal 60 stands proud of the upstanding lip 46a so that, when the closure plate 20 is moved into sealing engagement with the reaction vessel 40, fluid-tightness is effected by compression of the O-ring seal 60 between the underside of the closure plate 20 and the upper surface of the flange 46.

In view 2e, a variant is depicted in which the transverse flange 47 provided at the rim of the reaction vessel 40 is formed with a knife-edge annular protuberance 47a on its upper surface. A metal gasket 61 is placed over the flange 47 so that it overlies the knife edge protuberance

47a. The metal gasket 61 is of a thickness such that it stands proud of the upper surface of the supporting plate 30 so that, when the closure plate 20 is moved into sealing engagement with the reaction vessel 40, fluid-tightness is effected by compression of the gasket 61 between the underside of the closure plate 20 and the upper surface of the flange 47. Also, the closing action causes the knife-edge protuberance 47a to bite into the material of the gasket 61, ensuring seal integrity.

The embodiments described above with reference to views 2a to 2e all use a supporting plate 30 having a stepped through-bore which forms a shelf for the respective flange formations of the various reaction vessels that have been described. In view 2f, a plain supporting plate 30 is used and the reaction vessel 40 has a plain transverse flange 48. In this variant, the sealing plate 20 is provided on its underside with a cavity 22 which accommodates the O-ring seal 60. The O-ring seal 60 protrudes slightly from the cavity 22 so that, when the closure plate 20 is moved into sealing engagement with the reaction vessel 40, fluid-tightness is effected by compression of the O-ring seal 60 between the underside of the closure plate 20 and the upper surface of the flange 48.

View 2g is a variant of the embodiment described above in relation to view 2f, but incorporating a septum 23 in a through-hole in the sealing plate 20 which aligns with the opening at the top of the reaction vessel 40. The septum 23 enables sampling and/or dosing of the reaction vessel contents without compromising seal integrity. It will be understood by persons skilled in the art that a septum of equivalent construction could be incorporated in the embodiments discussed above with reference to views 2a to 2e.

View 2h shows another variant of the arrangement depicted in view 2f, this time incorporating a bursting disc 24 in a recess 25 formed in the walls of a through-hole provided in the sealing plate 20. Again, the through-hole in the sealing plate 20 is aligned with the opening at the top of the reaction vessel 40. The bursting disc 24 is an added safety precaution that may be required when operating with reactants under high pressure or where high pressures are likely to be created under the prevailing reaction conditions in the reaction vessel 40. Again, it will be understood by persons skilled in the art that the bursting disc feature could be incorporated in any one of the arrangements described above with reference to views 2a to 2e.

In yet another variant (not shown), the reaction vessels 40 may be sealed to the supporting plate 30 rather than to the closure plate 20. In this variant, the seals may be located on the underside of the reaction vessel flanges. However, this leaves a leak path from one reaction vessel to another which requires auxiliary seals to be provided between the supporting plate and the closure plate, surrounding the rim of each reaction vessel. Although functionally equivalent to the arrangements described above, this is complex and the simpler alternative of sealing the reaction vessels to the closure plate is preferred.

Although the invention has been particularly described above with reference to specific embodiments, it will be understood by persons skilled in the art that further modifications and variations are possible without departing from the scope of the claims which follow.

CLAIMS:

1. Apparatus comprising a plurality of reaction vessels, support means for supporting said reaction vessels, and a closure member adapted for movement relative to said support means such that it can be urged towards a rim of each of the reaction vessels to effect a fluid tight union between the reaction vessels and the closure member, wherein said reaction vessels have a flange at or adjacent to the rim and a seal associated with the flange.

2. Apparatus as claimed in claim 1, further comprising a temperature-controlled block movable relative to the underside of the support means to enable the reaction vessels to be accommodated within a uniform heating and/or cooling environment.

3. Apparatus according to claim 1 or claim 2 in which the reaction vessels are tubular.

4. Apparatus according to any preceding claim, in which at least some of the reaction vessels are provided with inert linings.

5. Apparatus according to any preceding claim in which the seals are gaskets composed of compressible materials.

6. Apparatus according to claim 5 in which the seals are O-ring seals.

7. Apparatus according to claim 5 in which the seals are metal gaskets formed of brass, gold, tantalum or indium.

8. Apparatus according to any one of claims 1 to 4 in which the seals are formed of a material capable of forming a knife-edge which, when subjected to the closing force exerted by the closure member, bites into the material of the flange and/or of the closure member.

9. Apparatus according to any one of claims 1 to 4 in which the flanges are formed with a knife-edge which bites into the material of the seals.

10. Apparatus according to any preceding claim in which the closure member incorporates inlets and outlets for liquids and/or gases.

11. Apparatus according to any preceding claim wherein

the closure member incorporates inlets for sensors.

12. Apparatus according to any preceding claim wherein the closure member incorporates gate means for overhead stirring.

13. Apparatus according to any preceding claim, wherein the closure member incorporates septum means in alignment with each of the reaction vessel openings.

14. Apparatus according to any preceding claim, wherein the closure member incorporates bursting disc means in alignment with each of the reaction vessel openings.

15. Apparatus according to any preceding claim, wherein the closure member has active or passive cooling means.

16. Apparatus according to any one of claims 2 to 15, in which the closure member maintains good thermal contact with the temperature-controlled block and is heated thereby to a temperature above which reagents condense on the underside of the closure member.

17. Apparatus according to any preceding claim, in which the closure member is moved relative to the support means

by manual, mechanical, electrical *via* a motor, hydraulic, or pneumatic means.

18. A process for performing physical and/or chemical operations in which use is made of an apparatus according to any one of the preceding claims.

19. A process according to claim 18 in which a mixing operation is carried out using an orbital shaker.

20. A process according to claim 19 in which use is made of rod-shaped stirrers present in the reaction vessels during mixing.

21. A process according to claim 18 in which a mixing operation is performed using ultrasound to initiate and maintain mixing.

22. A process according to any one of claims 18 to 21 in which a heating operation is performed.

23. A process according to any one of claims 18 to 22 in which a cooling operation is performed.

24. Apparatus substantially as described herein with

reference to the drawings.

25. A process for performing physical and/or chemical operations substantially as described herein with reference to the drawings.

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Application No:	GB 0100096.7	**Examiner:**	Michael Young
Claims searched:	1-25	**Date of search:**	17 October 2001

Patents Act 1977
Search Report under Section 17

Databases searched:

UK Patent Office collections, including GB, EP, WO & US patent specifications, in:

UK Cl (Ed.S): B1X (X8, X20)

Int Cl (Ed.7): B01J 3/00, 3/03, 3/04, 19/00; B01L 3/00

Other: ONLINE: WPI, EPODOC, JAPIO

Documents considered to be relevant:

Category	Identity of document and relevant passage		Relevant to claims
X	WO 95/27196 A1	(SANADI) see p.4 Statement of Invention, p.5 para.2, p.15 para. 2 (lines 12-16 in particular relating to claims 11 and 13) & para.3, fig.1 features 4,11,22,2, fig.3c. features 58, 59 & 60.	1,3,5, 11 &13

X	Document indicating lack of novelty or inventive step	A	Document indicating technological background and/or state of the art.
Y	Document indicating lack of inventive step if combined with one or more other documents of same category.	P	Document published on or after the declared priority date but before the filing date of this invention.
		E	Patent document published on or after, but with priority date earlier than, the filing date of this application.
&	Member of the same patent family		